



MODERN CONCEPTS IN THE PATHOGENESIS AND DIAGNOSIS OF CHRONIC PELVIC PAIN IN GYNECOLOGY

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Abstract: Chronic pelvic pain (CPP) in gynecology is a complex multifactorial syndrome involving neurophysiological, inflammatory, hormonal, and psychological components. It affects up to 15% of women of reproductive age and significantly reduces quality of life. The article presents a modern understanding of the etiology and pathogenesis of CPP, emphasizing peripheral and central sensitization, hormonal modulation of pain perception, and the interaction between the nervous and immune systems. Particular attention is given to endometriosis as the leading cause of CPP, as well as diagnostic challenges due to the absence of specific biomarkers and the limitations of non-invasive imaging. The article highlights the importance of an interdisciplinary and personalized approach combining pharmacological, surgical, and psychotherapeutic methods for effective management and prevention of chronicity.

Keywords: chronic pelvic pain, endometriosis, pain sensitization, gynecology, neurophysiology, diagnosis, estrogen, inflammation.

СОВРЕМЕННЫЕ ПРЕДСТАВЛЕНИЯ О ПАТОГЕНЕЗЕ И ДИАГНОСТИКЕ ХРОНИЧЕСКОЙ ТАЗОВОЙ БОЛИ В ГИНЕКОЛОГИИ

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Аннотация: Хроническая тазовая боль (ХТБ) в гинекологии представляет собой сложный многофакторный синдром, включающий нейрофизиологические, воспалительные, гормональные и психоэмоциональные компоненты. Она встречается у 15% женщин репродуктивного возраста и существенно снижает качество жизни. В статье представлены современные взгляды на этиологию и патогенез ХТБ, с акцентом на периферическую и центральную сенситизацию, гормональную модуляцию восприятия боли и взаимодействие нервной и иммунной систем. Особое внимание уделено эндометриозу как основной причине тазовой боли, а также трудностям диагностики из-за отсутствия специфических биомаркеров и ограниченных возможностей неинвазивных методов визуализации. Подчеркивается необходимость междисциплинарного и персонализированного подхода, сочетающего фармакологическое, хирургическое и психотерапевтическое лечение для повышения эффективности терапии и профилактики хронизации боли.

Ключевые слова: хроническая тазовая боль, эндометриоз, сенситизация боли, гинекология, нейрофизиология, диагностика, эстрогены, воспаление.

GINEKOLOGIYADA SURUNKALI TOS OG'RIG'NING PATOGENEZI VA DIAGNOSTIKASI BO'YICHA ZAMONAVIY QARASHLAR

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Annotatsiya: Ginekologiyada surunkali tos og'rig'i (STO) — neyrofiziologik, yallig'lanish, gormonal va psixologik omillarni o'z ichiga olgan murakkab ko'p omilli sindromdir. U reproduktiv yoshdagi ayollarning 15 foizigacha uchraydi va hayot sifatini keskin pasaytiradi. Maqolada STO etiologiyasi va patogenezining zamonaviy talqinlari, periferik va markaziy sezuvchanlikning oshishi, og'riqni gormonal boshqarilishi hamda asab va immun tizimlari o'rtasidagi o'zaro ta'sir yoritilgan. Endometriozi — asosiy sabab sifatida, shuningdek, biomarkerlarning yo'qligi va noinvaziv diagnostika usullarining cheklanganligi tufayli yuzaga keladigan tashxis qiyinchiliklariga alohida e'tibor qaratilgan. Samarali davolash va og'riqning surunkalashuvini oldini olish uchun farmakologik, jarrohlik va psixoterapevtik yondashuvlarni birlashtirgan shaxsiylashtirilgan, ko'p tarmoqli yondashuv zarurligi ta'kidlanadi.

Kalit so'zlar: surunkali tos og'rig'i, endometriozi, og'riq sezuvchanligi, ginekologiya, neyrofiziologiya, diagnostika, estrogen, yallig'lanish.

Intoroduction. According to the International Association for the Study of Pain (IASP), "pain is an unpleasant sensation and emotional experience associated with actual or potential tissue damage or described in terms of such damage. " Pain is a necessary defense mechanism, signaling both the onset of damage to the integrity of external and internal tissues and organs, and the danger of further damage. As a stress factor, pain is accompanied by a negative psychoemotional reaction, which stimulates actions aimed at eliminating the cause of this negative sensation, which is its primary physiological meaning. But pain is not only a psychophysiological phenomenon; it is a crucial symptom of a variety of acute and chronic diseases, so complaints of pain should guide the physician to find its cause. Another aspect of pain is its significant impact on a person, significantly reducing quality of life. It is no coincidence that in Russian, the words "bol" and "bolezni" (disease) share the same root. While acute pain carries a significant physiological burden, chronic pain is pathological by definition. Chronic pelvic pain is pain in the pelvic region that lasts at least 2 weeks of each month for 6 months or more [1]. Among localized pains, pelvic pain exhibits the greatest gender differences, allowing it to be considered a uniquely female problem [2]. It occurs in 38 out of 1,000 women aged 15–38, i.e., more often than migraine (21 out of 1,000), and is comparable in frequency to asthma (37 out of 1,000) or chronic back pain (41 out of 1,000). The incidence of chronic pelvic pain reaches 15% of the population. Chronic pelvic pain is the reason approximately 4% of women seek medical attention, and in gynecological clinics, it determines the indication for 12% of all hysterectomies and over 40% of diagnostic laparoscopies. The incidence of pain-related morbidity is steadily increasing. For example, among girls and young women in the Russian Federation, the incidence of pelvic pain has increased 1.5-fold, with an overall increase in gynecological pathology from 30.8% to 44.2% [3]. Etiology and pathogenesis of pain. All anatomical structures of the pelvis are potential sources of pain. In addition to the uterus and appendages, pain signals can be generated by the bladder, intestines, pelvic floor muscles, skin, and components of the peripheral and central nervous systems. Many patients have multiple causes of pain. Although chronic pelvic pain is a symptom rather than a disease, it rarely reflects a single pathological process. Even if there is an obvious primary source of pain, its pathogenesis most often involves inflammatory or neuropathic changes in the central and/or peripheral nervous system, and this is one of the reasons for which many patients with chronic pelvic pain have several different diagnostic conclusions. In such cases, it is reasonable to consider chronic pelvic pain as a diagnosis, not a symptom, and pain-associated conditions as pain triggers. The sensation of pain is a complex phenomenon involving peripheral and central mechanisms [1]. Pain sensitivity of somatic structures (e.g., muscles, skin, bones) is mediated by nociceptors, which are represented by undifferentiated nerve endings of myelinated A-delta and unmyelinated C-fibers that respond to mechanical, chemical, and thermal stimuli. These stimuli, converted into an electrical impulse in sodium/potassium channels, are transmitted as a wave of depolarization along afferent sensory neurons and initiate the release of neurotransmitters at a synapse with second-order neurons located in the dorsal horn of the spinal cord. Second-order neurons include low-threshold mechanoreceptors, high-threshold nociceptors, and wide dynamic range (WDR) neurons, represented by A-delta, partially A-beta, and C-fibers. Pain signals from the uterus, bladder, and, partially, the vagina, as well as the muscles and skin of the pelvic floor, are

transmitted by sympathetic afferents, which also form synapses in the dorsal horn. The pelvic peritoneum contains three categories of nociceptors, whose action is realized exclusively through the sympathetic nervous system. Visceral nociceptors do not respond to stimuli associated with direct injury but are highly sensitive to tension, stretch, ischemia, and inflammation. Visceral pain is poorly localized because it does not directly project to the cerebral cortex. Well-localized pain is usually of somatic or neuropathic origin. Chronic pain develops as a result of peripheral and central sensitization of the nervous system. The sensitivity of peripheral nociceptors is increased by inflammatory neurotransmitters such as CGRP (calcitonin gene-related peptide), substance P, histamine, prostaglandins, and bradykinin. This mechanism for the development of chronic pelvic pain is characteristic of endometriosis and interstitial cystitis. Another important factor in peripheral sensitization is abnormal or excessive functioning of nerve endings. Peripheral nerve damage is associated with a greater loss of small C-fibers than large A-beta fibers, which, accordingly, develop new branches, replacing vacant C-fiber spaces in the substantia gelatinosa of the spinal cord. This may contribute to the development of allodynia, when light touch is perceived as pain. The activity of nociceptors is determined by a number of factors, among which the expression of nerve growth factor (NGF) is of great importance, which in turn depends on estrogen stimulation and the expression of the WT1 gene, which ensures, among other functions, neuronal development [4]. Increased NGF production leads to an increase in the number of receptors affiliated with demyelinated C-fibers and peripheral sensitization. Thus, estrogen stimulation should be considered as a possible factor in increased pain sensitivity, along with a genetic predisposition to an excessive pain response. This partly explains the female "privilege" for pain and the dependence of pain on fluctuations in hormonal levels during different phases of the menstrual cycle and periods of a woman's life. Diseases of the pelvic organs are associated with nociceptive visceral pain. However, due to the viscerosomatic reflex, stimulation of visceral nociceptors can lead to the formation of a focus of irritation in the muscles of the lower abdomen and pelvic floor [5]. Activation of sympathetic efferents causes contraction of muscle fibers, forming trigger points. These pathophysiological processes determine the persistence of local pain even after the elimination of its primary cause. A direct correlation has been observed between the number of painful episodes associated with pelvic pathology and a lowered pain threshold. The development of chronic pelvic pain syndrome is impossible without central sensitization. WDR neurons mediate these changes in the central nervous system. Neurons in the spinal sensory loop, constantly exposed to painful stimuli, become stimulated, facilitating the release of nociceptive neurotransmitters that lower the threshold for synaptic activation. In pathological conditions, WDR neurons are capable of forming abnormal synapses, spreading across various regions of the dorsal horn in response to injury or neuroinflammation. Activation of silent synapses in the dorsal horn and glia further contributes to central sensitization. Central sensitization causes the pain zone to extend beyond the primary injury site, creating a zone of referred pain. Affective pain is mediated by neurotransmitters and involves signals from various areas of the brain (thalamus, hypothalamus, reticular formation, medulla oblongata and midbrain, limbic structures). Pain modulation, leading to its reduction, is achieved by opioids, γ -aminobutyric acid, neurokinin I, and norepinephrine. Impaired activity of the antinociceptive system plays a significant role in maintaining chronic pain status and serves as a mechanism for the development of behavioral and emotional disorders, anxiety, and depression. Chronic pelvic pain and depression. The pathogenetic relationship between depression and chronic pain is not fully understood, but there is a hypothesis that their commonality is associated with the insufficiency of cerebral serotonergic systems. On the other hand, stress, anxiety, fear, and depression make a person more susceptible to pain [6]. Patients suffering from chronic pelvic pain are more likely than healthy women to experience such psychologically negative events as divorce, family troubles, and violence. Stress plays a particular role in the development of depression and simultaneously leads to increased anxiety, which is accompanied by muscle tension and can activate at least one component of pain aggravation. On the other hand, the dissociation between the subjective severity of pain and the uncertainty or lack of evidence of its organic cause becomes an additional stressor for women [7], negatively impacting their emotional state and contributing to the development of depression. Thus, the development of chronic pain is a complex pathophysiological

mechanism, only partially dependent on its underlying cause. However, chronic pelvic pain does not strike a patient overnight; its development takes months and years. A woman with dysmenorrhea, a patient with a history of pelvic inflammatory disease (PID), and many other women who periodically experience pelvic pain risk developing a difficult-to-treat condition that is highly likely to develop if the patient and her physician fail to promptly address the body's initially rare, but over time increasingly persistent, signals of trouble. Symptoms of the neuropathic component of pain cannot be attributed solely to the nervous system: for example, allodynia in the lower abdomen and perineum is significantly more common in women with gynecological problems [8]. In general, the nature of the pain, its location, radiation, causes, and methods of relief aid in diagnostic evaluation but cannot provide a reliable diagnosis of the underlying disease, or even the presence of such a disease. Endometriosis as one of the causes of chronic pelvic pain. There is no doubt that the most common cause or accompaniment of chronic pelvic pain in women is endometriosis, a disease associated with the growth of endometrial-like tissue outside the uterus, which affects approximately 10% of women of childbearing age, ranks third among gynecological diseases in terms of hospitalization frequency and first in terms of indications for hysterectomy [9]. Two main symptoms are characteristic of endometriosis: pelvic pain and infertility. In the presence of chronic pelvic pain, endometriosis is detected in 71% of cases, the combination of chronic pelvic pain and infertility is caused by endometriosis in 84% of patients. The pathogenesis of pain in endometriosis includes several mechanisms [10]: inflammation, adhesion, fibrosis, deep damage with nerve involvement. The primary pathophysiological component of pain is considered to be an abnormal (excessive) inflammatory response characteristic of the disease, which is accompanied by an increased release of pain mediators, particularly prostaglandins. At the same time, proinflammatory cytokines (tumor necrosis factor, interleukin-6), chemokines, and immune cell products (CCL2, CCL3, CCL5, etc.) exert their influence both directly through the inflammatory pain response and through and indirectly – by increased pain sensitivity of neuronal cells. An early symptom of endometriosis is dysmenorrhea. Dyspareunia is usually associated with damage to the retrocervical region and/or uterosacral ligaments. Non-cyclic pelvic pain, pain during ovulation, and a variety of painful symptoms from the gastrointestinal tract and urinary tract during menstruation are very likely. Severe pelvic pain is often associated with deep invasive endometriosis. Endometriosis is called an "overlooked" disease, and this makes it similar to chronic pelvic pain syndrome. Retrospective analysis has shown that on average 7-12 years pass from the onset of the first manifestations of the disease and the patient's complaints to diagnosis [11]. This is facilitated by objective and subjective factors, but above all, by the peculiarities of the accepted diagnostic criteria. A mandatory condition for diagnosing endometriosis is direct visualization of the implants during laparoscopy, preferably with morphological verification (in case of deep infiltrating endometriosis and ovarian endometriomas, histological examination of the excised tissue is mandatory). Without surgical diagnosis, endometriosis remains only a guess. But indications for laparoscopy in patients with chronic pelvic pain are limited: • infertility combined with chronic pelvic pain; • severe (unbearable) chronic pelvic pain; • signs of deep infiltrating endometriosis; • endometrioma larger than 4 cm; • no effect of empirical hormonal therapy for chronic pelvic pain within 3 months. The search for non-invasive markers for early detection of the disease is underway. For example, data have been obtained on an increase in interleukin-6 and 8 in endometriomas [12], but the increase in the expression of proinflammatory cytokines is too nonspecific to be used in practice. Sensitive and specific biomarkers of endometriosis have not yet been found, and none of the proposed methods have demonstrated accuracy sufficient for its integration into clinical practice [13]. Radiological diagnostic methods (computer and magnetic resonance tomography, positron emission tomography) are suitable only for identifying infiltrative and cystic forms of endometriosis [14, 15], where their sensitivity reaches 98%. Sonography performed by transrectal and vaginal access and the use of 3D sensors also provide satisfactory visualization of endometriomas [16]. But even using highly sensitive indirect visualization methods, a physician cannot definitively diagnose endometriosis before surgery. As a result of this practice, doctors either make false diagnoses or do not make any diagnoses at all [17].

Conclusion. Chronic pelvic pain (CPP) represents a multifactorial and interdisciplinary problem in modern gynecology, combining neurophysiological, endocrine, inflammatory, and psychosocial components. It arises not as a simple symptom but as a complex syndrome reflecting both peripheral and central sensitization of pain pathways. The transition from acute to chronic pain is mediated by persistent nociceptive stimulation, hormonal modulation (particularly estrogen-dependent nerve growth factor expression), and neuroplastic changes in the spinal cord and brain, leading to altered pain perception and emotional distress.

Endometriosis remains the most frequent etiological factor, though numerous other pelvic and extrapelvic sources may contribute to chronic pain. The presence of comorbidities—such as depression, anxiety, and muscular dysfunction—further aggravates the clinical course and complicates management. Despite progress in imaging and molecular diagnostics, the identification of specific biomarkers for CPP and endometriosis remains elusive, making laparoscopy with histological verification the gold standard.

The effective management of CPP requires a multimodal and personalized approach that includes pharmacological, surgical, physiotherapeutic, and psychological interventions. Early recognition of pain triggers, timely diagnosis, and addressing both somatic and psychosocial factors are crucial to prevent chronicity and improve patients' quality of life. A multidisciplinary framework involving gynecologists, neurologists, psychologists, and pain specialists offers the most promising outcomes in reducing the burden of chronic pelvic pain among women.

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